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(54) PRODUCTION OF SOLUTIONS

(71) We, INGERTHORPE HOLDINGS LIMITED, a British Company, 26, North John Street, Liverpool L2 9RX, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention relates to a method of and apparatus for producing aqueous solutions for medical purposes.

The present invention is intended to be the subject of a Patent Of Addition to British Patent Application No. 26679/72, Serial No. 1 450 030, which describes and claims a process for the production of an aqueous solution of desired concentration for medical purposes which comprises passing water through a reverse osmosis column capable of retaining 100 percent of pyrogenic material, and subsequently, in either order, passing the water through a sterilizer capable of eliminating 100 percent of bacterial material and admixing, in suitable ratio, the water with a desired material, or with a solution of such material of higher concentration than desired.

Specification 26679/72 Serial No. 1 450 030 also describes and claims an apparatus for the production of an aqueous solution of desired concentration for medical purposes, which comprises a reverse osmosis column capable of retaining 100 percent of pyrogenic material, the outlet from which is connected, in either order, to the inlet of a sterilizer capable of eliminating 100 percent of bacterial material, and to a proportioning system.

The present invention provides a process for the production of an aqueous solution of desired concentration for medical purposes which comprises passing water through a reverse osmosis column capable of retaining 100 per cent of pyrogenic materials, preheating the water in a preheater, passing the pre-heated water to a main steriliser in which the solution is maintained at a sterilising temperature for sufficient time to sterilise the water and either prior to said preheating step or after said sterilising step admixing the water, in a suitable ratio, with a solution of higher concentration than desired.

Advantageously the water is preheated to a temperature of substantially 135°C.

Conveniently the higher concentration solution is prepared from water which has undergone the sterilising step.

The present invention also provides apparatus for the production of an aqueous solution of desired concentration for medical purposes, which comprises a reverse osmosis column capable of retaining 100% of pyrogenic material; a steriliser capable of eliminating 100% of bacterial material; and a proportioning system; the steriliser having a pre-heater coupled to the reverse osmosis column for pre-heating pyrogen free water therefrom and a main steriliser for sterilising said pyrogen free water.

Advantageously the proportioning system comprises a variable ratio mix pump for mixing said pyrogen free water with a solution of higher concentration than desired to produce said desired concentration solution, and a sensor for monitoring the concentration of the pump output solution the sensor being connected downstream of the pump and operable to control the operation of the pump in dependance upon the monitored concentration.

The present invention is further described hereinafter, by way of example, with reference to the accompanying drawing which is a schematic diagram of an apparatus for producing an aqueous solution for medical purposes.

The apparatus shown in the drawing includes an inlet 10 for connection to a source of water (not shown in the drawing) e.g.

tap water; a pump 20 which maintains an adequate flow rate of water to two reverse osmosis columns 24 which are capable of retaining 100% of pyrogenic materials; a proportioning system 40 which mixes the pyrogen free water with a pyrogen free, mineral free, sterile, concentrated solution of the material required (e.g. glucose or glycine) and then delivers solution at the required concentration to a steriliser 50 which sterilises the solution; and a solution outlet 70 which, in this embodiment, is connected to a bottling plant 72 e.g. a laminar flow filling and capping machine. The aforementioned parts of the apparatus are in the main water flow path through the apparatus. The pump 20 may be omitted if the water pressure from the source is sufficient to maintain an adequate flow rate of water to the reverse osmosis columns 24. Furthermore, although two reverse osmosis columns 24 are shown, the actual number used will depend upon the output flowrate of solution required from the apparatus. Water flows from the inlet 10 by way of a deioniser 12 which deionises the water and a meter 16 for measuring the conductivity of the water to the pump 20, a filter 14 conveniently being provided between the inlet 10 and the pump 20 to filter out material which might damage the pump 20. The deionised water is pumped to the reverse osmosis columns 24 conveniently via a second filter 22 which is included to protect the reverse osmosis columns 24 and is usually a mechanical filter for removing relatively large particles, the filter having a pore size between 0.5 and 10 microns, preferably between 0.5 and 1 micron. The high water pressure developed in the reverse osmosis columns 24 by the pump 20 cause the water to permeate through the semi permeable membranes of the columns 24 while the membranes prevent the passage of pyrogenic material. To prevent damage to the reverse osmosis columns 24 as a result of pressure build up therein the pyrogen-containing water is fed back to the input of the pump 20 by way of a feedback network which includes a return tank 26. The reverse osmosis columns 24 are connected to the tank 26 by way of three paths one of which is controlled by a valve 28, a second of which is controlled by a pressure responsive valve 30 in series with a valve 32 and a third of which, also controlled by the pressure responsive valve 30, includes a heat exchanger 34 further described hereinafter. The tank 26 also has an overflow connected to an outlet 36 controlled by a valve 38.

Pyrogen free water from the reverse osmosis columns 24 passes preferably through a filter 42 of the proportioning system 40 to a variable ratio mix pump 44. The filter 42 is a safety device with means for measuring the pressure differential between the two sides of the filter. Thus if the reverse osmosis column fails this additional filter will begin to block and the pressure differential between the two sides of the filter will alter considerably. Preferably the apparatus includes an arrangement whereby any alteration in the pressure differential from its normal range causes the apparatus to be switched off. The filter is preferably a surface type filter and a suitable pore size is of the order of 0.2μ. As an additional safety feature or an alternative to the means for measuring the pressure difference across the filter 42 a pressure head safety device may be included in the apparatus to ensure correct pressure. The pump 44 mixes the pyrogen free water with the concentrated solution of the material required to produce an aqueous solution of the desired concentration. This desired concentration is monitored by a sensor 46, connected downstream of the pump 44, which controls the pump 44 accordingly to ensure that the desired concentration is maintained.

The pyrogen free solution then flows into the steriliser 50 which comprises a pre-heater 52 for pre-heating the solution to a temperature of approximately 135°C and a main steriliser 54 which is connected downstream of the pre-heater.

The pre-heater is advantageously designed so that the exposure time of the solution to the pre-heating is short and may be in the form of a concentric tube heater. The main steriliser 54 is advantageously an autoclave and preferably comprises a pipe through which the solution flows and which is immersed in a fluid bath. The pipe is arranged in the bath in a multitube parallel flow system so that the solution flowing therethrough is subjected to a sterilising temperature for sufficient time to sterilise the solution, the fluid bath being maintained at for example 138°C. Conveniently the sterilised solution is passed through a heat exchanger 56 connected upstream of the pre-heater 52 to further pre-heat solution upstream of the pre-heater 52 e.g. to 90°C. Where the sterilised solution is to be bottled, as in the present example, it is advisable for the sterilised solution to be at or above approximately 80°C to ensure that any bacteria in the bottling plant which might contaminate the solution are killed. To this end a heater 58 is provided downstream of the heat exchanger 56 to heat the cooled solution up to a temperature of approximately 80°C. A pressurising valve 60, which conveniently has a bypass valve 62, is connected downstream of the heater 58 to reduce the risk of the solution boiling, and the valve 60 is connected to the outlet 70 by way of a further valve 64 and a filter 66.

The apparatus also has a further inlet 80 which is connected to an overflow of the bottling plant 72 and enables feed of the overflow solution to the tank 26 and/or the steriliser 50. The heat exchanger 34 is provided to cool the overflow solution to a temperature at whch it can be recycled through the sterliser 50 and connects the inlet 80 to a recirculating pump 82 which returns the overflow solution to the main water flow path between the proportioning system and the heat exchanger 56. The heat exchanger 34 also connects the inlet 80 to the tank 26 by way of a pressure relief valve 84.

The pyrogen free, mineral free, sterile, concentrated solution is supplied to the variable ratio mix pump 40 from a vessel 90 conveniently by way of a filter 92 and a valve 94. The vessel 90 is connected in a closed loop from the valve 64 so that it receives only pyrogen free, sterilised solution and concentrate in the form of a powder charge is added to the solution in the vessel 90 to produce the concentrated solution.

One disadvantage of previous known apparatus for producing aqueous solutions for medical purposes lies in the possibility of bacteria entering the apparatus while it is switched off, particularly at the output 70, and contaminating the solution produced during use of the apparatus. To overcome this disadvantage a reservoir 96 of 1% formalin solution is connected to various parts of the water main flow path by way of an injection pump 98 and valves 100. Immediately the apparatus is switched off the injection pump 98 operates to fill the apparatus with the formalin solution, the latter displacing the water in the apparatus and killing bacteria which enters the apparatus. On switch on of the apparatus the bottling plant is maintained inoperative to allow the water flowing via the inlet 10 to flush the formalin solution out of the apparatus through the drain outlet 36. After a few minutes delay the powder charge is released in the vessel 90 and the bottling plant operated.

Where the outlet 70 is connected to a drip feed for a patient it is essential that the solution supplied should be at the correct temperature, approximately 40°C. The heater 58, and therefore the cooler 34, may be omitted, or alternatively the heater 58 may be used to regulate the solution temperature to approximately 40°C. The outlet 70 and the inlet 80 may then be directly connected.

In further embodiments in accordance with the present invention the vessel 90 is replaced by a source of ready made concentrate solution, and the deioniser 12 may be eliminated if deionised water is supplied to the inlet 10.

The proportioning sytem may alternatively be connected in the main flow path downstream of the steriliser.

The main steriliser may alternatively be a flash steriliser in which the water is heated rapidly to 150°C to 160°C for substantially 1 minute and then cooled to 30°C to 40°C.

WHAT WE CLAIM IS:—

1. A process for the production of an aqueous solution of desired concentration for medical purposes which comprises passing water through a reverse osmosis column capable of retaining 100 per cent of pyrogenic materials, preheating the water in a preheater, passing the pre-heated water to a main steriliser in which the solution is maintained at a sterilising temperature for sufficient time to sterilise the water and either prior to said preheating step or after said sterilising step admixing the water, in a suitable ratio, with a solution of higher concentration than desired.

2. A process as claimed in claim 1 wherein the water is admixed with said higher concentration solution prior to said preheating.

3. A process as claimed in claim 1 or 2 wherein the water is preheated to a temperature of substantially 135°C.

4. A process as claimed in claim 1, 2 or 3 wherein said higher concentration solution is prepared from water which has undergone the sterilising step.

5. A process as claimed in claim 1, 2, 3 or 4 wherein the water is deionised prior to being passed through the reverse osmosis column.

6. A process as claimed in any of claims 1 to 5 wherein the main steriliser is a flash steriliser.

7. A process as claimed in claim 6 wherein the water is heated rapidly in the main steriliser to 150°C to 160°C for substantially 1 minute and then cooled to 30°C to 40°C.

8. A process as claimed in any of claims 1 to 7 wherein the water is passed through a pre-filter prior to entering the reverse osmosis column.

9. A process as claimed in any of claims 1 to 8 wherein the temperature of the sterilised, mixed solution of desired concentration is adjusted to substantially 80°C.

10. Apparatus for the production of an aqueous solution of desired concentration for medical purposes, which comprises a reverse osmosis column capable of retaining 100% of pyrogenic material; a steriliser capable of eliminating 100% of bacterial material; and a proportioning system; the steriliser having a pre-heater coupled to the reverse osmosis column for pre-heating

pyrogen free water therefrom and a main steriliser for sterilising said pyrogen free water.

11. Apparatus as claimed in claim 10 wherein the proportioning system is connected between the outlet from the reverse osmosis column and the inlet to the pre-heater.

12. An apparatus as claimed in claim 10 or 11 wherein the main steriliser is an autoclave.

13. Apparatus as claimed in claim 10, 11 or 12 wherein the proportioning system comprises a variable ratio mix pump for mixing said pyrogen free water with a solution of higher concentration than desired to produce said desired concentration solution, and a sensor for monitoring the concentration of the pump output solution the sensor being connected downstream of the pump and operable to control the operation of the pump in dependance upon the monitored concentration.

14. Apparatus as claimed in any of claims 10 to 13 further comprising means for adusting the temperature of the sterilised, mixed solution of desired concentration to substantially 80°C.

15. Apparatus as claimed in claim 14 wherein said means comprises a heat exchanger having two flow paths one of which is connected upstream of said pre-heater and the second of which is connected downstream of said main steriliser, and a heater connected downstream of said second flow path and said proportioning system for heating the sterilised, mixed solution to substantially 80°C.

16. Apparatus as claimed in any of claims 10 to 15 further comprising a deioniser connected upstream of said reverse osmosis column for deionising the water fed to said column.

17. An apparatus as claimed in any one of claims 10 to 16, in which a pre-filter is located upstream of the reverse osmosis column.

18. An apparatus as claimed in claim 17 in which the pre-filter has a pore size between 0.5 and 10 microns.

19. An apparatus as claimed in claim 18, in which the pre-filter has a pore size between 0.5 and one micron.

20. An apparatus as claimed in any one of claims 10 to 19 which also comprises a pump connected upstream of said reverse osmosis column.

21. An apparatus as claimed in any one of claims 10 to 20 which also comprises a pressure head safety device to ensure correct pressure.

22. An apparatus as claimed in any one of claims 10 to 21, which also incorporates an additional filter between the outlet from the reverse osmosis column and the inlet to the steriliser and means for measuring the pressure differential between the two sides of the filter.

23. An apparatus as claimed in claim 22, in which the additional filter is a surface filter.

24. An apparatus as claimed in claim 22 or 23 in which the additional filter has a pore size of about 0.2μ.

25. An apparatus as claimed in any one of claims 22 to 24, which also includes a device for switching off the apparatus in the event that during operation the pressure differential between the two sides of the additional filter varies from its normal range.

26. Apparatus as claimed in any of claims 10 to 25 further comprising injection means operable responsively to deactivation of the apparatus to displace water in the apparatus with a fluid for killing bacteria.

27. Apparatus as claimed in claim 26 wherein said injection means is an injection pump and said fluid is formalin solution.

28. Apparatus as claimed in any of claims 10 to 27 whose output is connected to a bottling machine for bottling said aqueous solution, an overflow of the bottling machine being connected to a second input of the apparatus for feeding overflow solution into said apparatus upstream of the steriliser, the second input being connected to the steriliser upstream thereof by way of cooling means for reducing the temperature of said overflow solution.

29. Method for the production of an aqueous solution of desired concentration substantially as hereinbefore described with reference to the accompanying drawing.

30. Apparatus for the production of an aqueous solution of desired concentration constructed and adapted to operate substantially as hereinbefore described with reference to the accompanying drawing.

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1 SHEET

COMPLETE SPECIFICATION

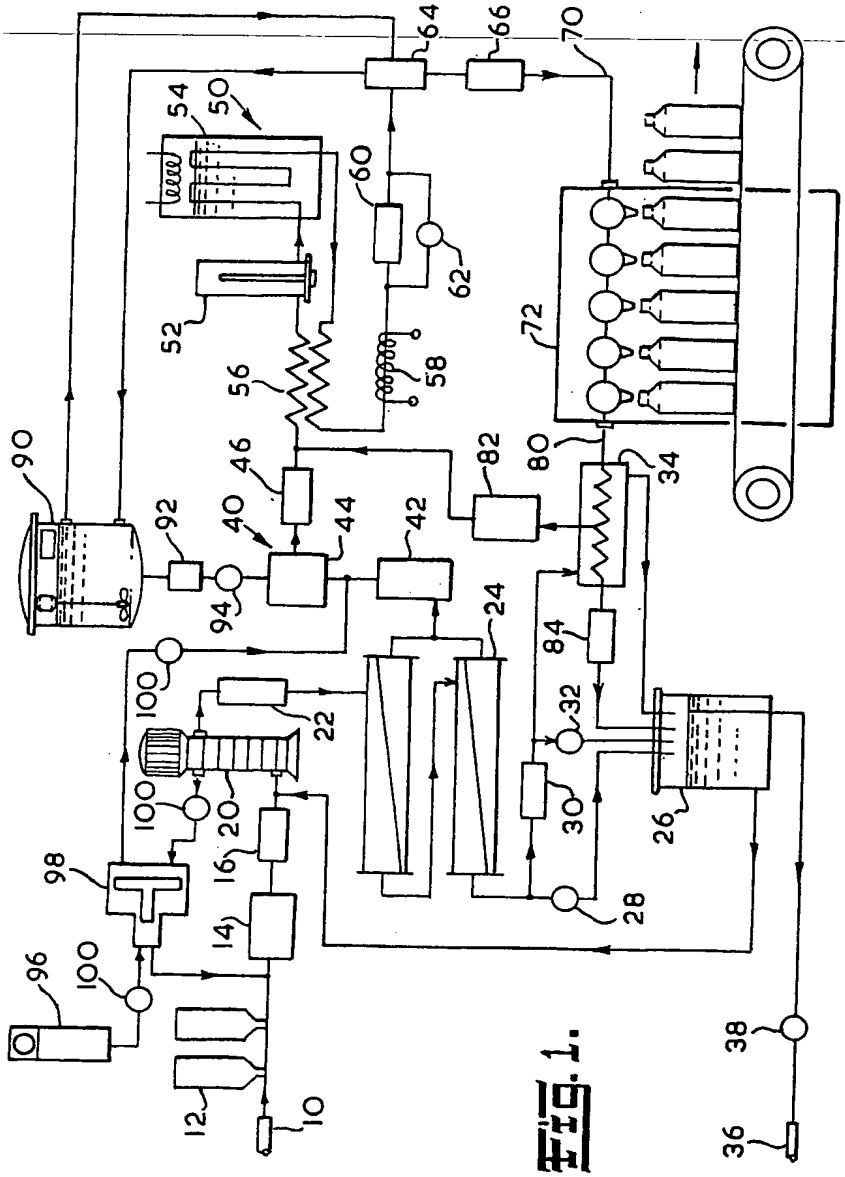

FIG. 1.